Prevention of Sudden Cardiac Death

Angel R. León, MD
Carlyle Fraser Heart Center
Division of Cardiology
Emory University School of Medicine

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Sudden Cardiac Death

Cardiac arrest predominantly occurs due to Ventricular Tachycardia or Fibrillation

Most VT or VF occurs independently of acute myocardial infarction

1 of 5 experiencing out-of-hospital cardiac arrest survive to hospital discharge

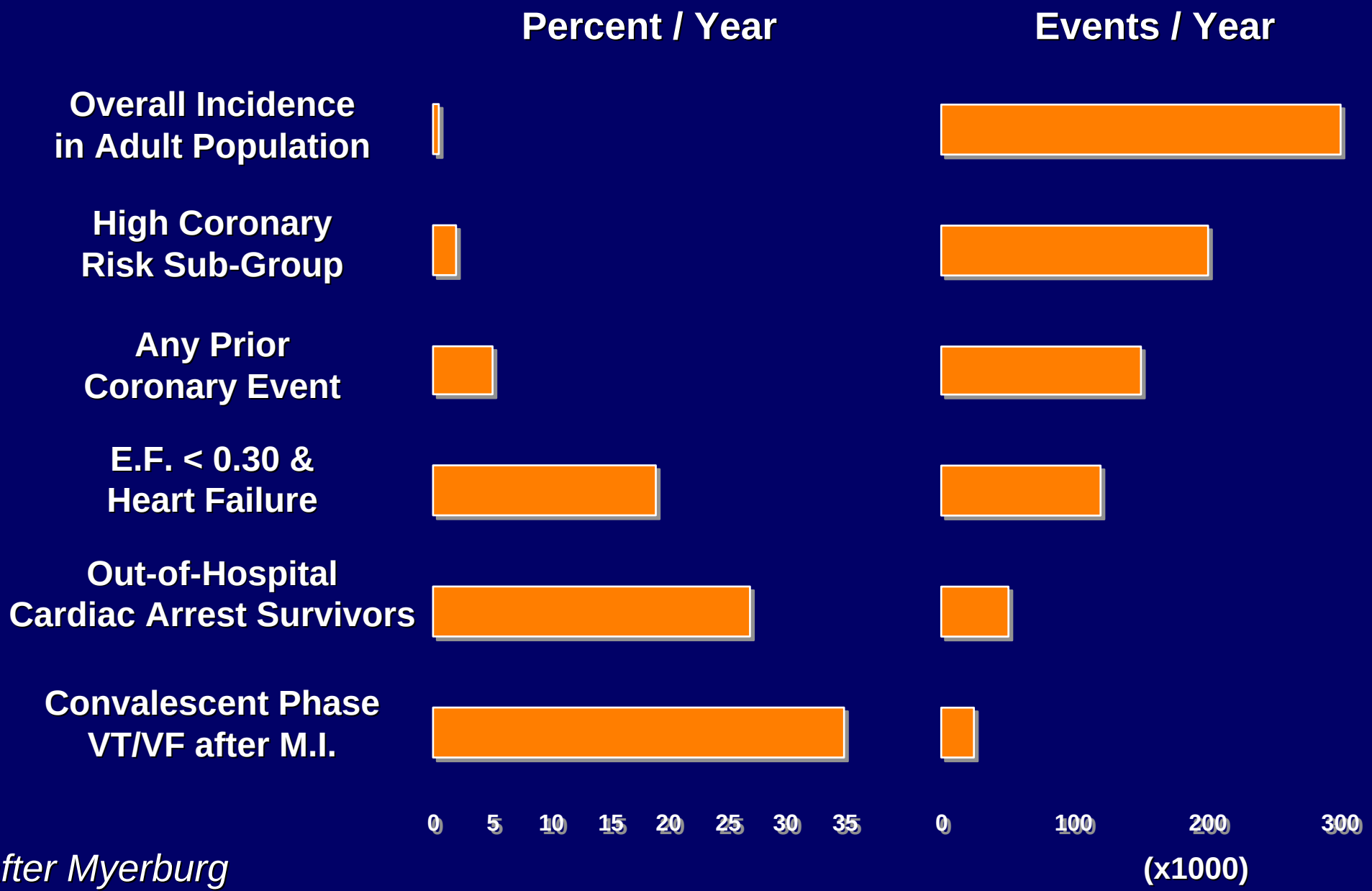
Preventing SCD: Logical Strategy

Identify the groups at highest risk

Determine the best therapy in each group

Allocate economic resources accordingly

Groups at Risk: Probability vs. Total Events



after Myerburg

Evolution of Therapy to Prevent SCD

ICD for survivors of SCD

ICD therapy for sustained VT

ICD in “high-risk” patients after EPS

Prophylactic ICD insertion

Question:

Will the ICD reduce all cause mortality in an individual with LV dysfunction as the only marker of risk?

MADIT II: EF $\leq$ 30% due to previous MI

SCD-HFT: EF $\leq$ 35% with or without CAD

MADIT-II: Eligibility

Chronic CAD with prior MI (> 30 days)

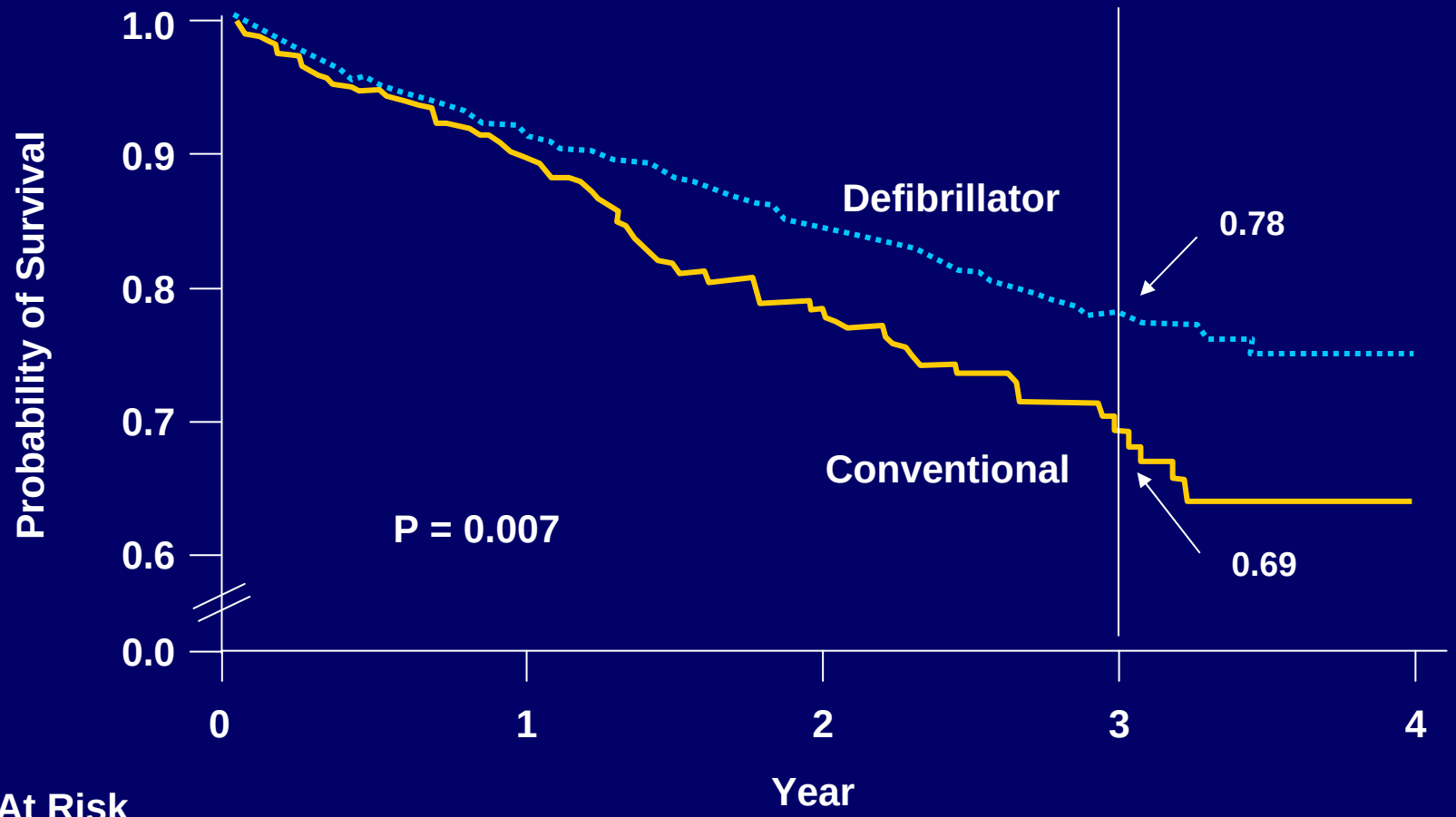
LVEF $\leq$ 0.30

No requirement for NSVT or EPS

No CABG or PTCA within 3 mos

Pts with syncope excluded

MADIT-II Survival Results



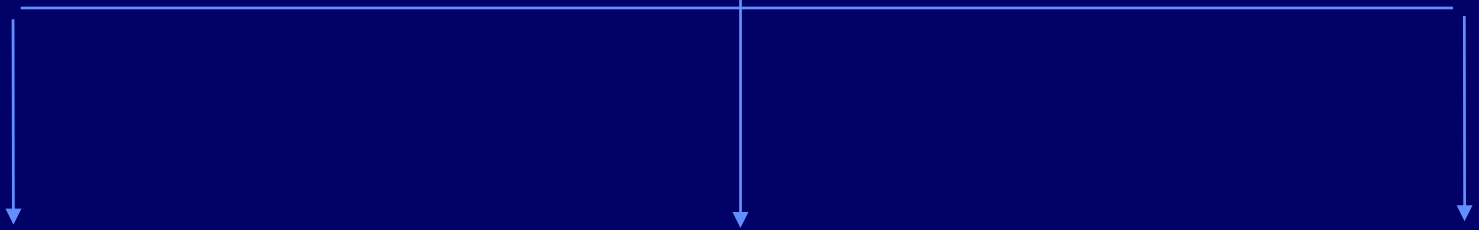
No. At Risk					
Defibrillator	742	502 (0.91)	274 (0.94)	110 (0.78)	9
Conventional	490	329 (0.90)	170 (0.78)	65 (0.69)	3

Moss AJ. *N Engl J Med*. 2002;346:877-83.

SCD-HeFT: Prophylactic ICD in CHF

Ishemic and Non-ischemic LV Dysfunction
LVEF ≤ 35%,
NYHA Class II or III CHF
N=2,521

Randomization



Conventional CHF Rx & placebo

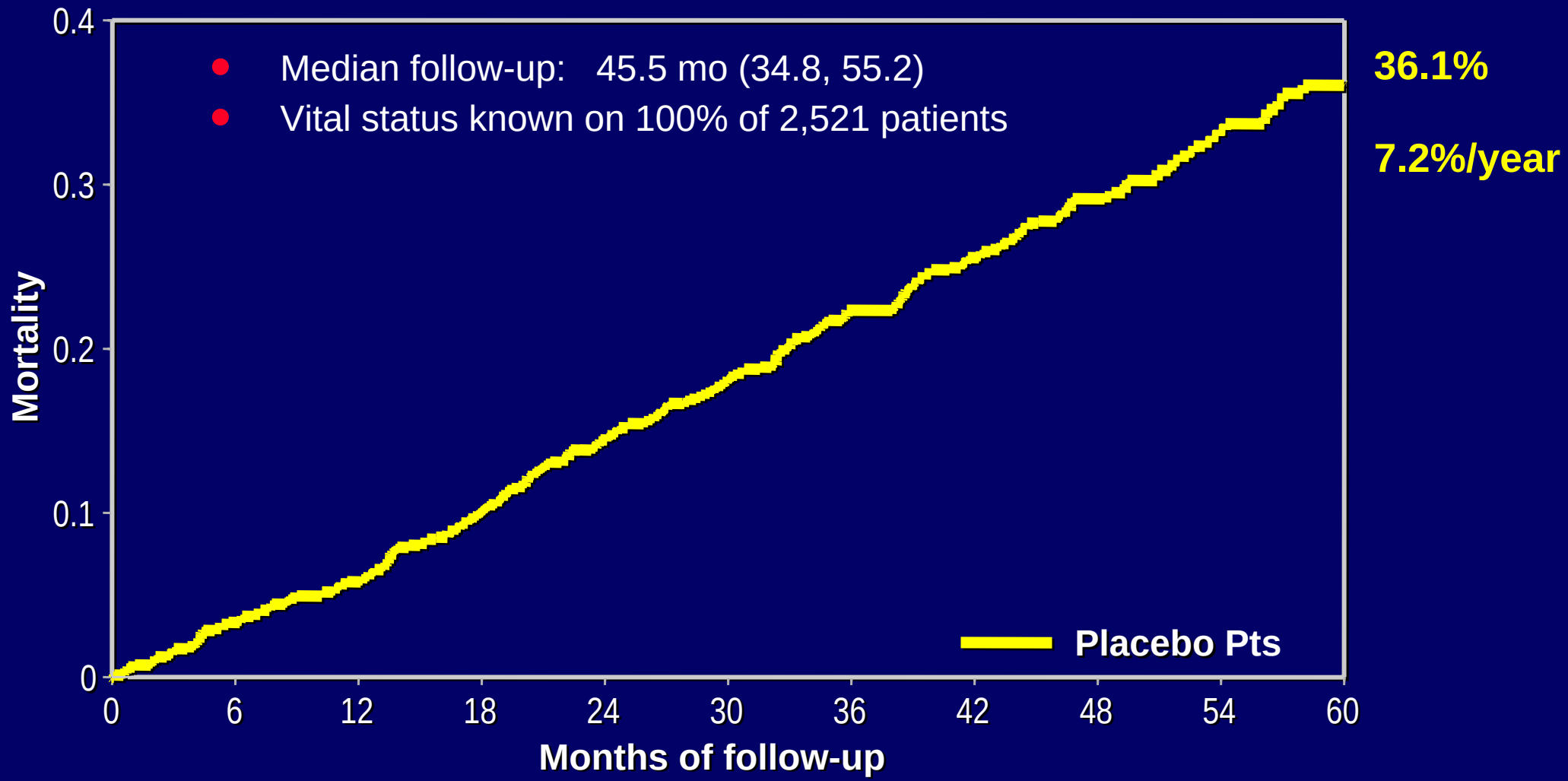
Conventional CHF Rx & amiodarone (double blind)

Conventional CHF Rx & ICD

Adapted from Bardy, et. al. NEJM 2005

Natural History of Class II-III CHF

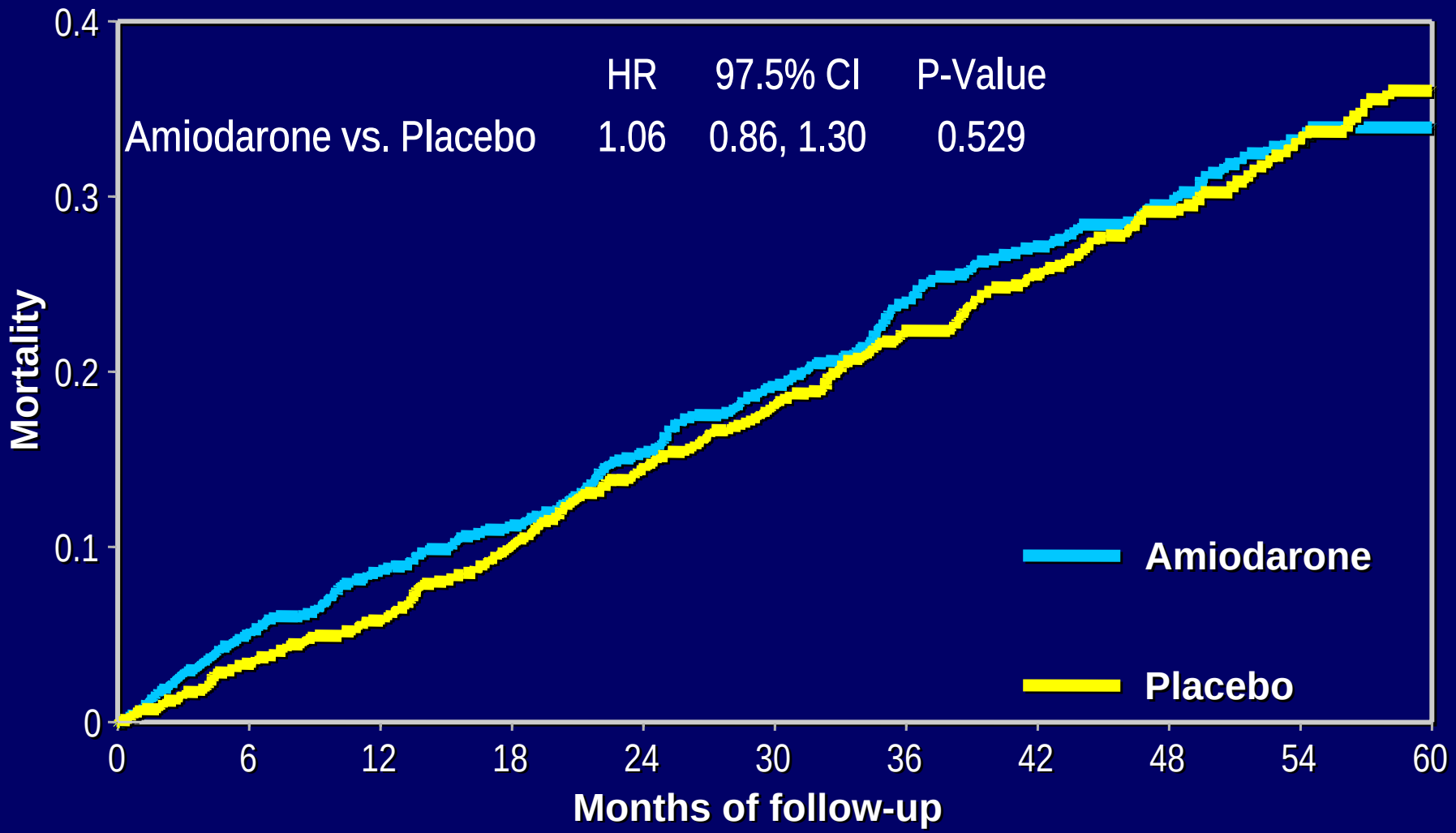
SCD-HeFT Optimal Medical Therapy



Adapted from Bardy, et. al. NEJM 2005

Amiodarone versus Placebo

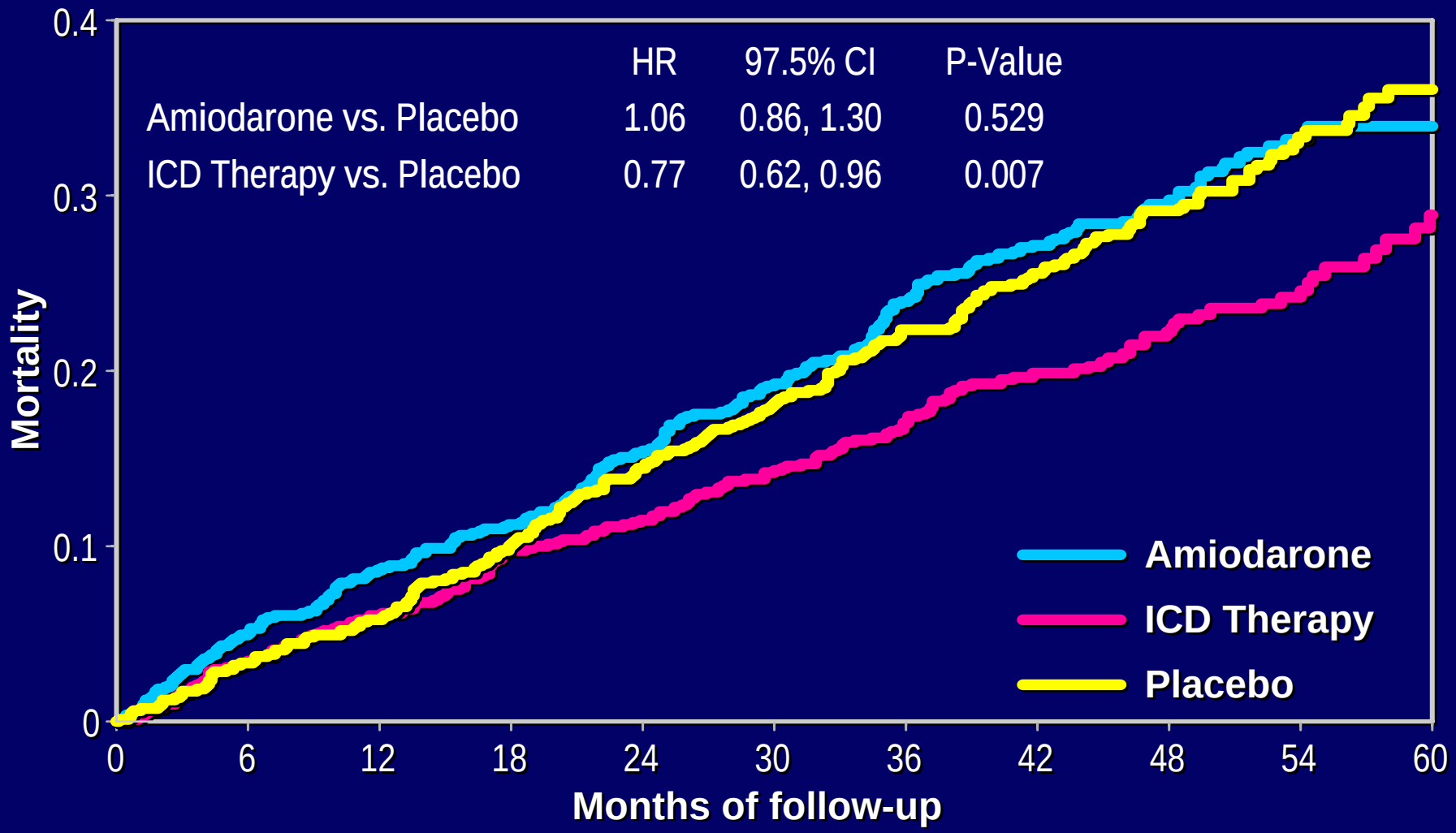
Intention-to-Treat



Adapted from Bardy, et. al. NEJM 2005

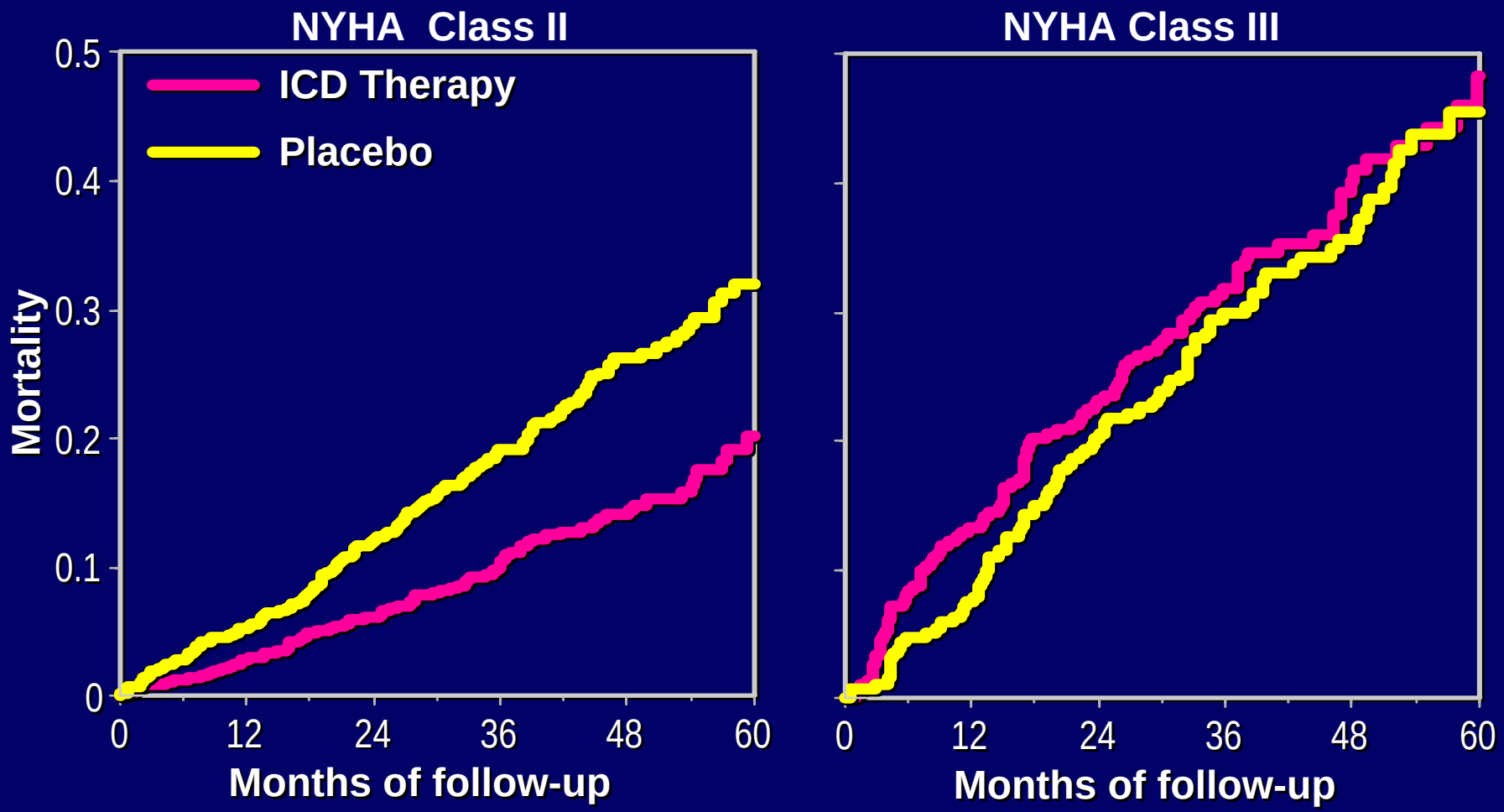
SCD-HeFT Treatment Group Mortality

Intention-to-Treat



Adapted from Bardy, et. al. NEJM 2005

ICD Impact by NYHA Class

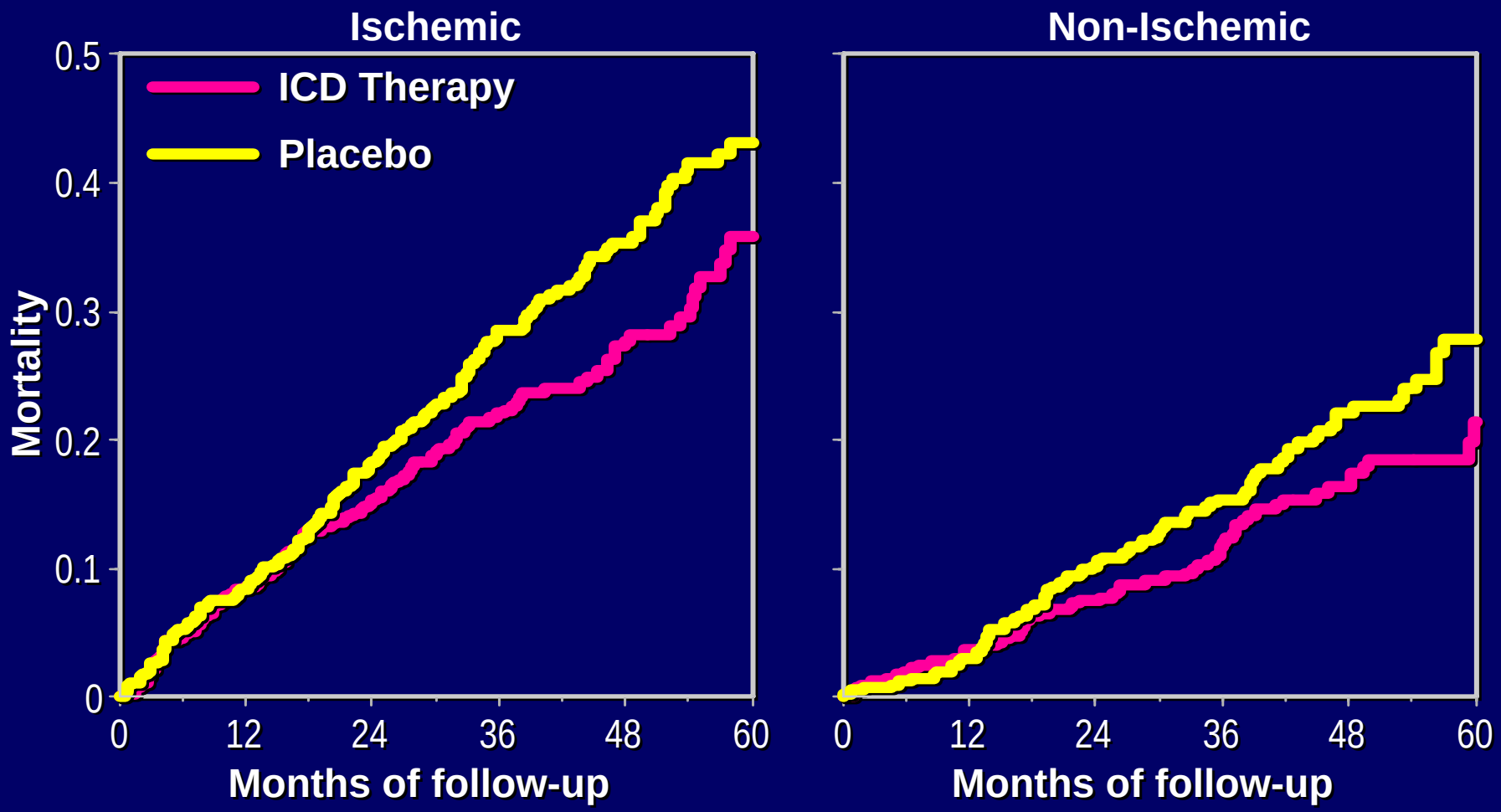


HR	97.5% CI
0.54	0.4-0.74

HR	97.5% CI
1.16	0.84-1.61

Adapted from Bardy, et. al. NEJM 2005

Primary Endpoint by CHF Etiology

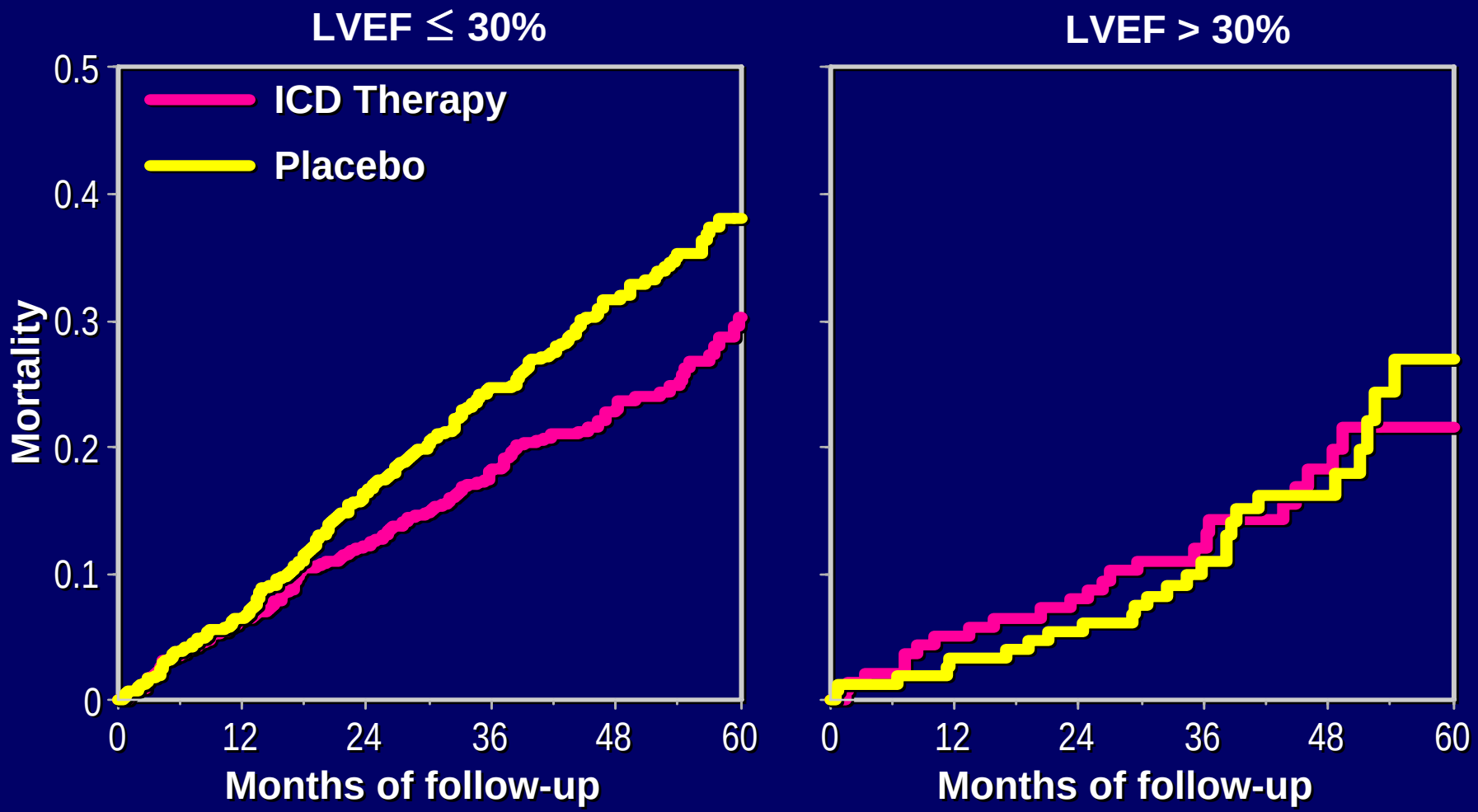


HR	97.5% CI
1.04	0.79-0.60

HR	97.5% CI
1.07	0.73-0.50

Adapted from Bardy, et. al. NEJM 2005

Impact of ICD According to LVEF



HR	97.5% CI
0.73	0.57-0.92

HR	97.5% CI
1.08	0.57-2.07

Adapted from Bardy, et. al. NEJM 2005

SCD-HeFT: Conclusions
EF < 0.35 Class II-III CHF

Medically treated patients experienced a 7.2% per year mortality over 5 years without an ICD

The ICD decreased relative mortality by 23%, with an absolute 7.5% reduction as primary prevention

Amiodarone did not improve survival in heart failure pts

Primary Prevention with the ICD

How many must we treat to save one life:

31% (med Rx) vs. 22% (ICD): Difference 9%

1/0.09 = 11

MADIT II:	**11 implants/life saved**
MADIT II QRS >150:	**4 implants/life saved**
SCD-HeFT:	**14 implants/life saved**

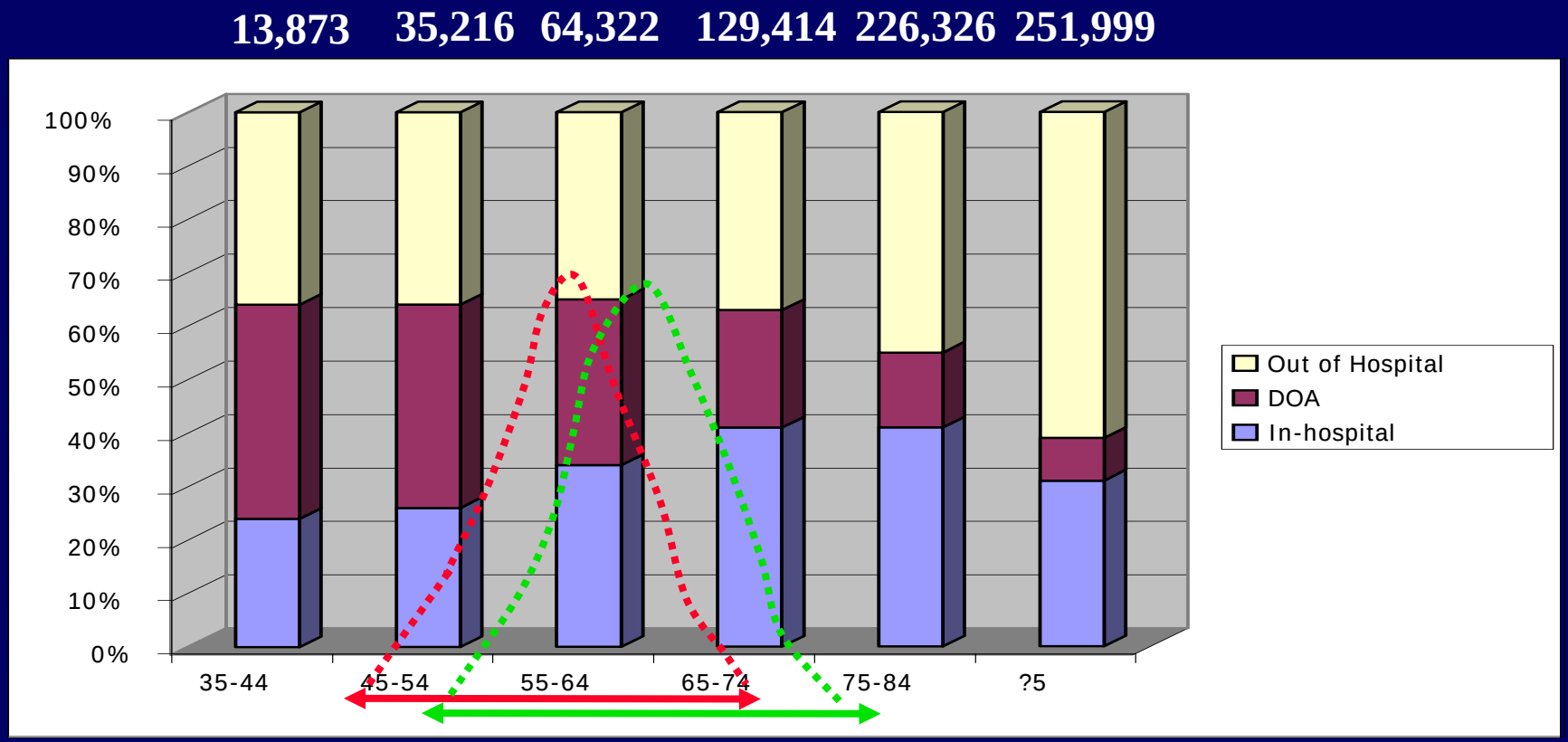
Clinical Characteristics:

	Age	LVEF	NYHA%
MADIT II	65 ± 10	0.22	40 (II), 60 (III)
SCD-HFT	60.1*	0.25	70 (II), 30 (III)

Exclusion criteria: Significant "co-morbid" conditions

** Median age, 50th, 75th %ile (51.7, 68.5)*

MADIT II and SCD-Heft: Age Context



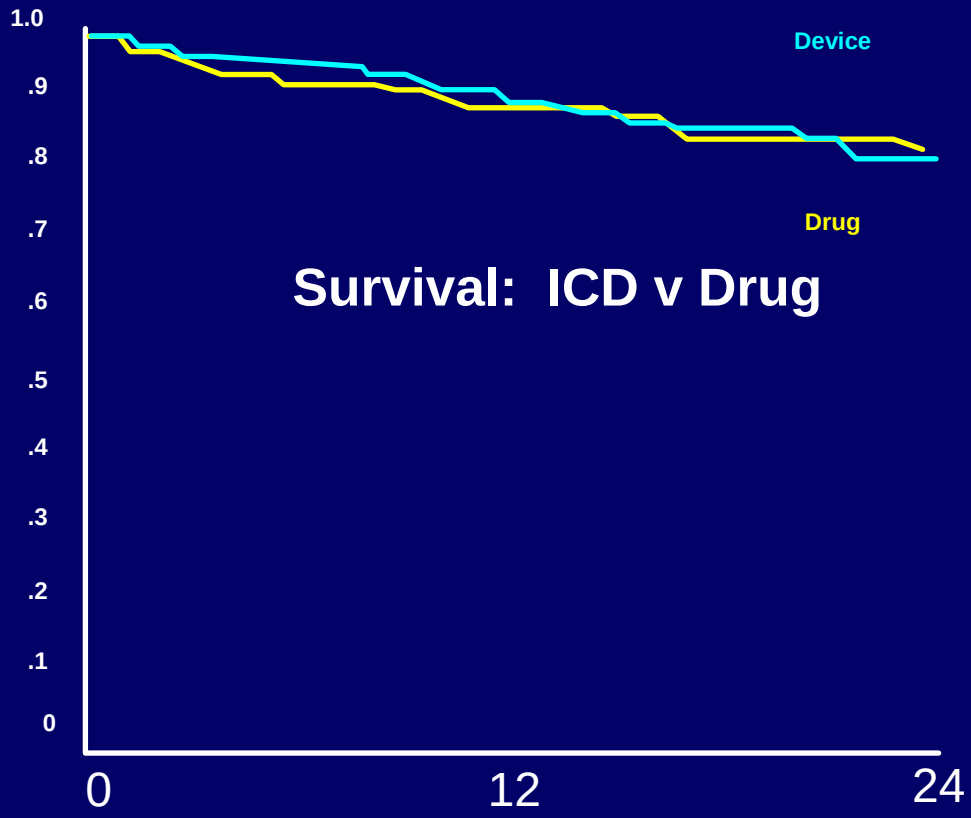
MADIT II: Mean Age 65 +/- 10 years

SCD-Heft: Median Age 61, [___, ___] 95% CI

MMWR Feb. 15, 2002

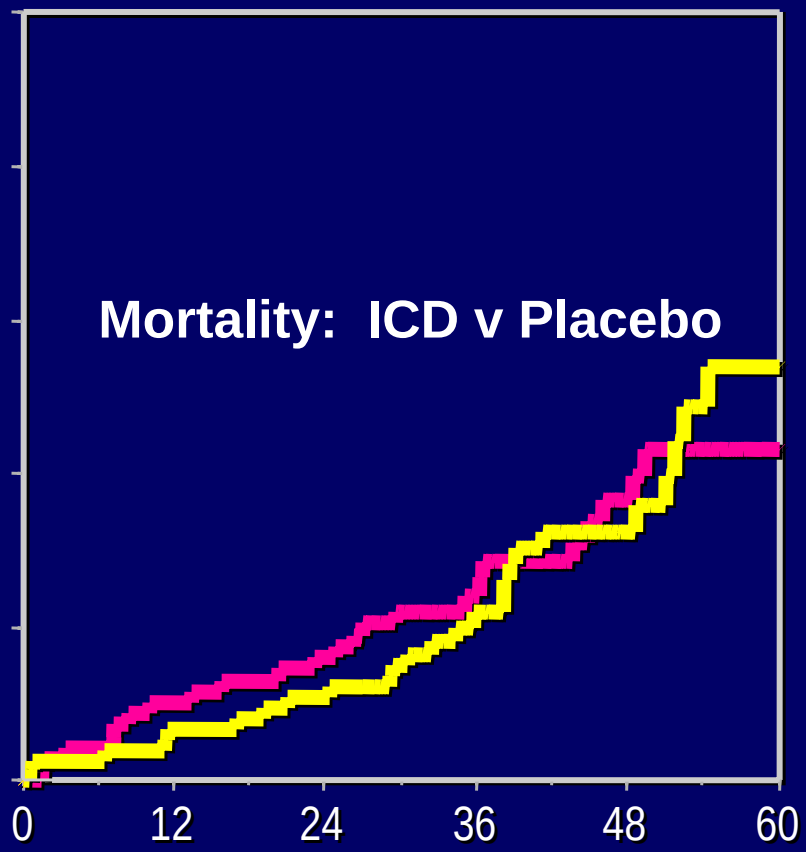
Stratifying ICD Impact by LVEF

AVID EF > 0.34



Survival: ICD v Drug

SCD-HeFT EF 0.30-0.35



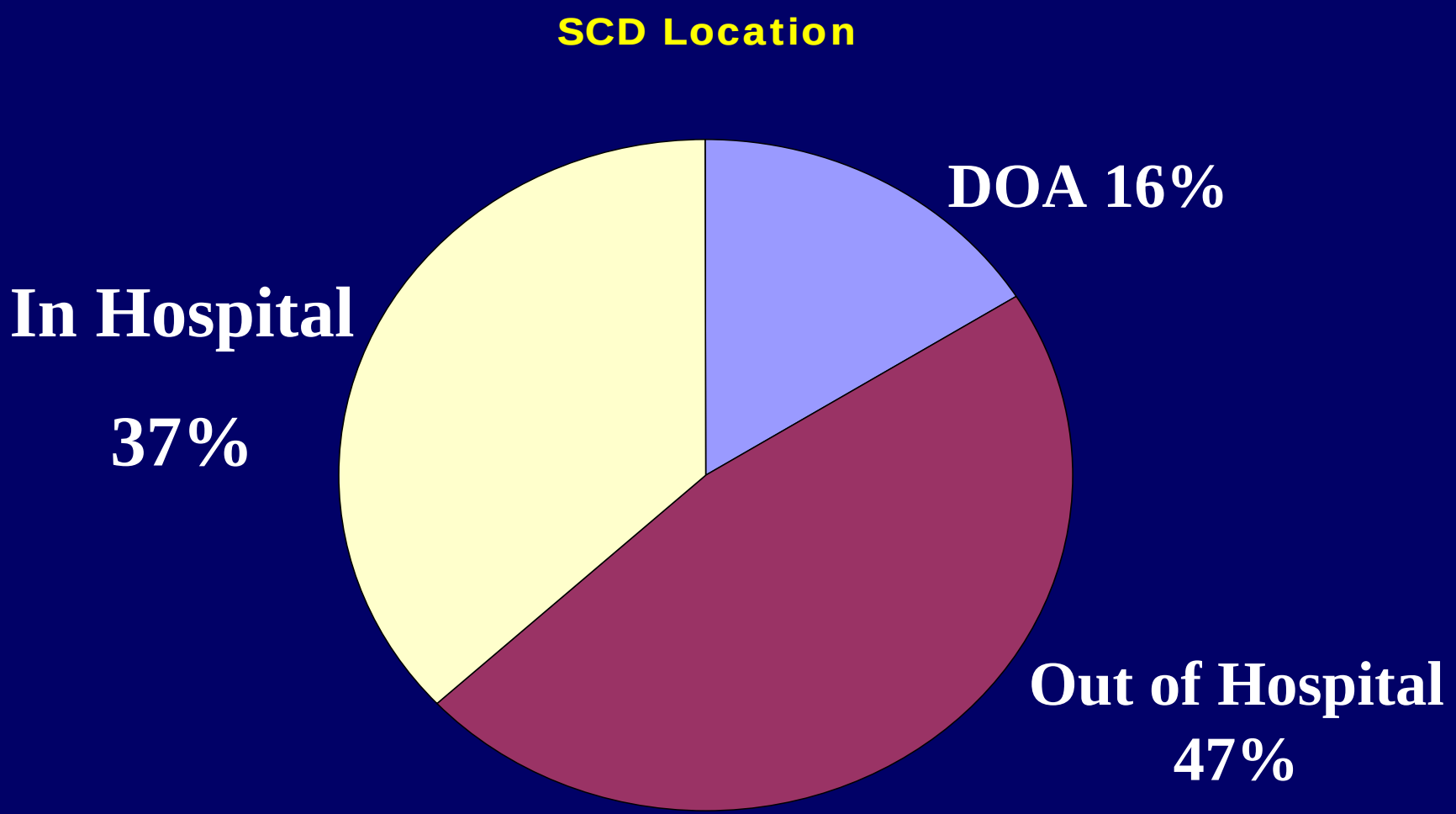
Mortality: ICD v Placebo

Stratification by Age and LVEF

	Age	LVEF	NYHA Class
MADIT II	65 ± 10	0.22	40/60
SCD-HFT	60.1*	0.25	70/30

Stratified Randomization would better analyze impact of therapy based on baseline EF, NYHA Class and age at entry.

SCD by Location: Would an ICD Help? (N = 462,000)



MMWR Feb. 15, 2002

Conclusions

SCD survivors, and those with spontaneous VT and EF < 0.35 benefit from ICD implant.

Pts with NSVT, MI, and EF 0.35-0.40 with induced VT benefit from ICD implant

Selected pts with low EF (≤ 0.35) benefit from ICD implant

Points for Debate

The ICD may not prevent in-hospital death or death from advanced disease, or aging:

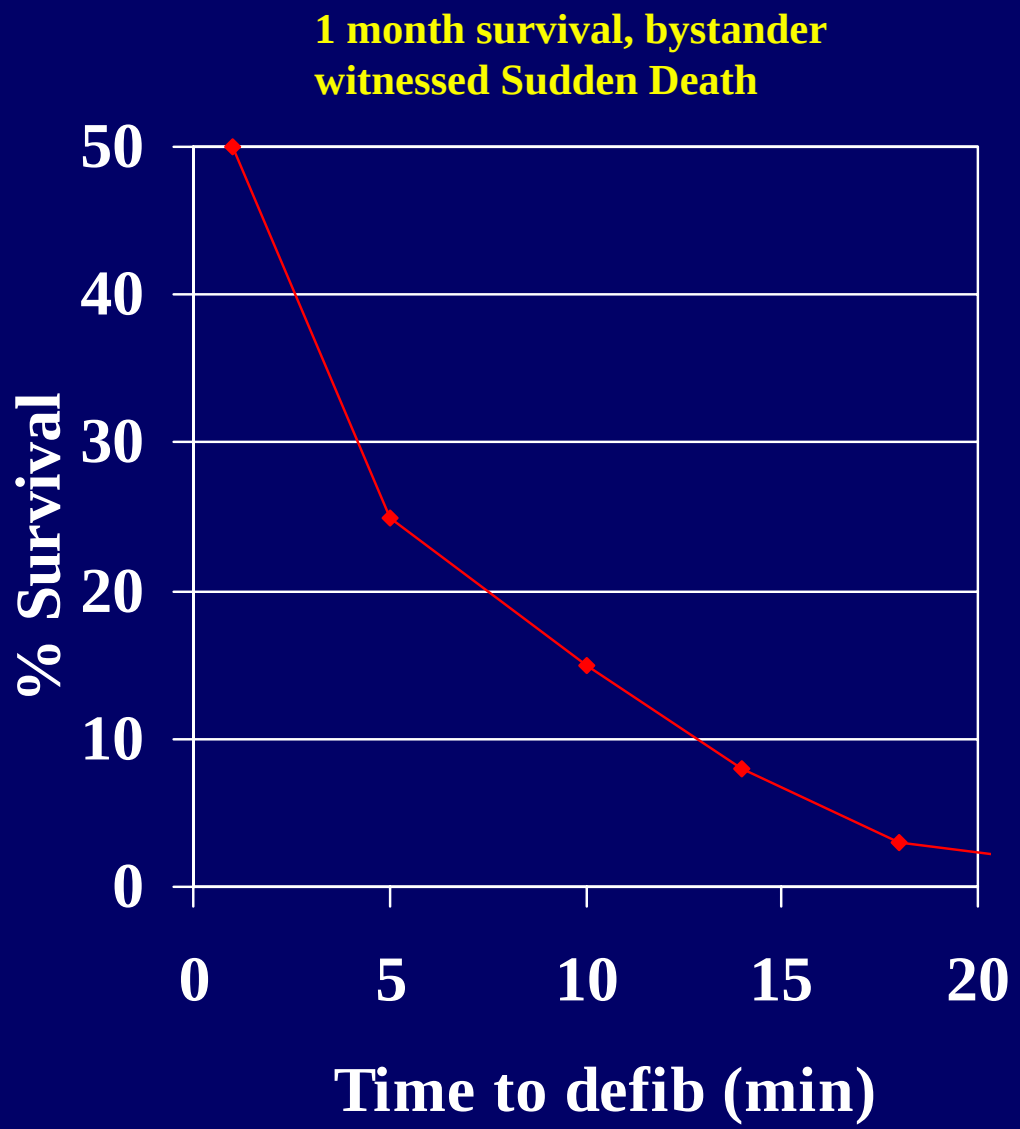
Should a patient with multiple co-morbidities receive an ICD?

Out-of-hospital SCD predominates in the later decades of life (>75yrs):

Can we extrapolate impact on survival?

Surviving SCD: Time is Life!

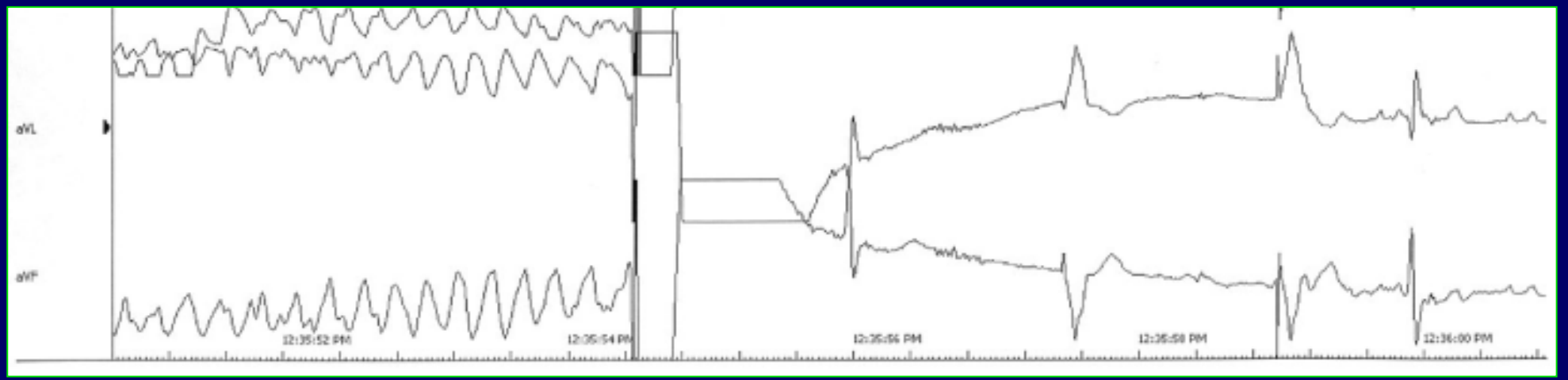
- 460,000 deaths per year
- Likelihood of surviving SCD is low
- Early shocks work
- Late shocks don't



Swedish Cardiac Arrest Registry
Am J Cardiol, 1999

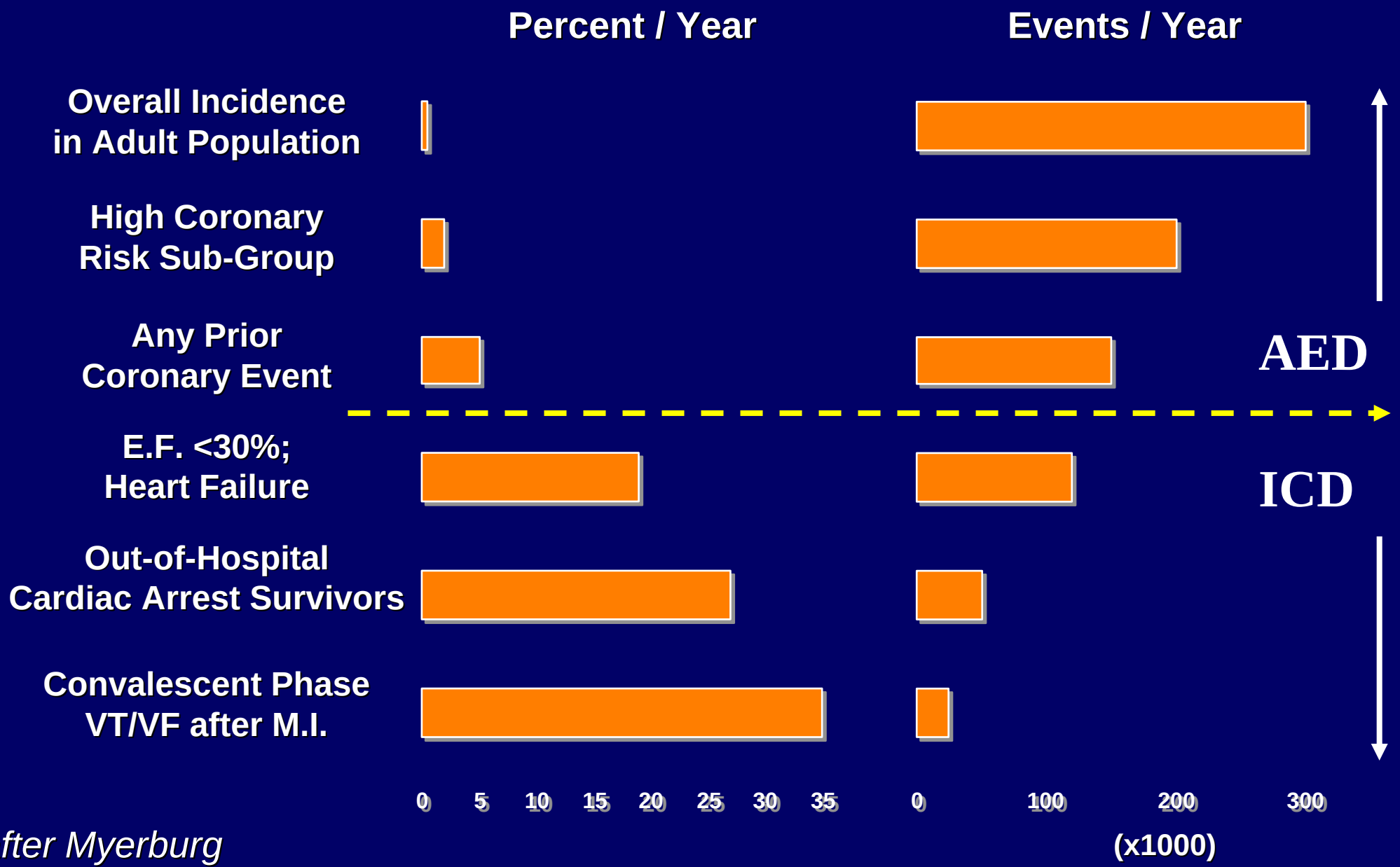
Effective Therapy for SCD:

Timely restoration of sinus rhythm: *Defibrillation*



How do we best distribute defibrillators?

Best Strategies to Prevent SCD



after Myerburg

Question:

How about a prophylactic ICD within 30 days after MI? (***MADIT II excluded recent infarcts***)

DINAMIT (n=674)

- **Acute MI and low EF: ICD vs. Medical Rx**
- **ICD reduced "arrhythmic mortality"**
- **ICD implant did not reduce total mortality**

Connolly, LBCT ACC 2003

Question:

Should a pt with 3-vessel CAD and LV dysfunction undergoing CABG also get an ICD?

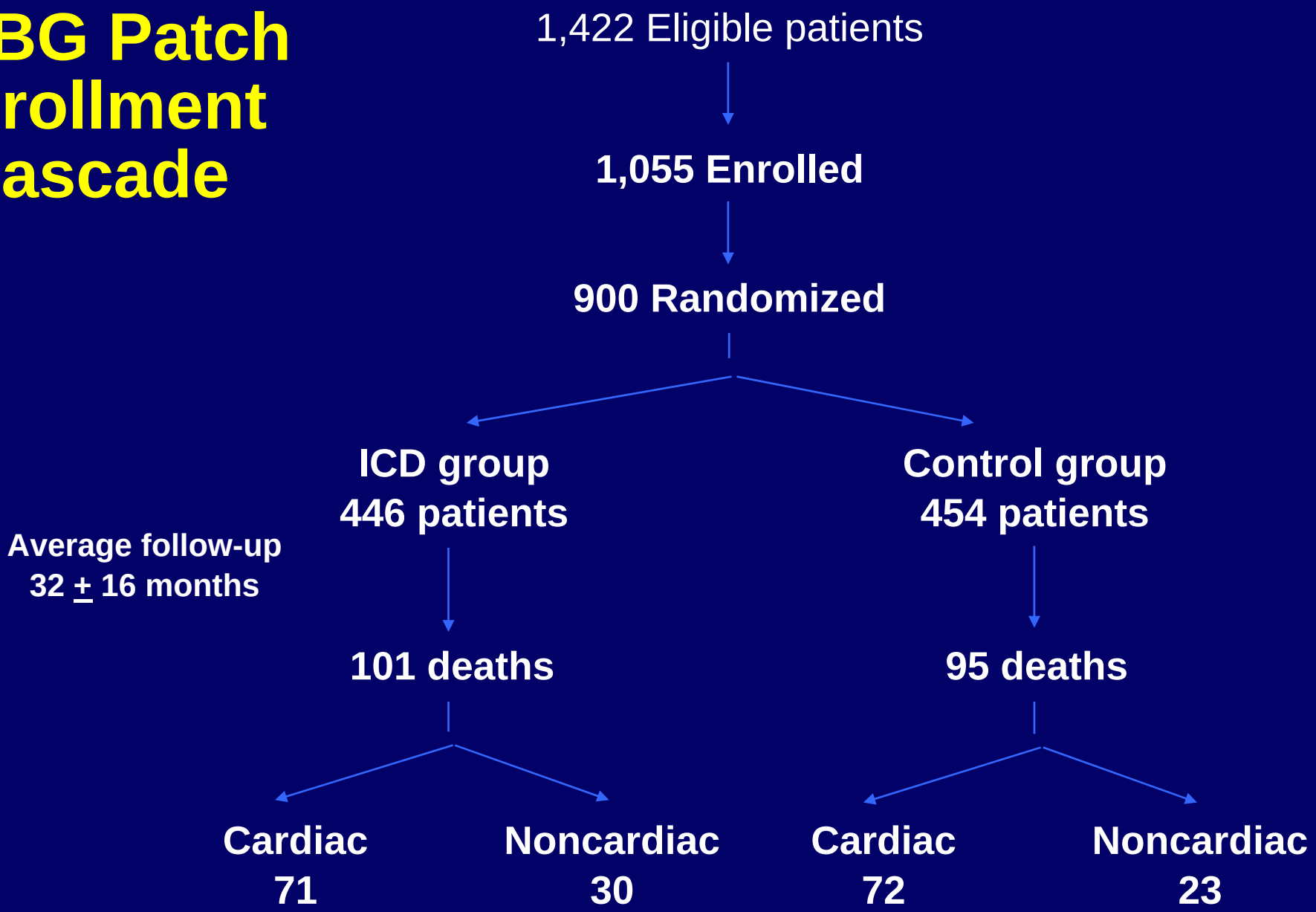
CABG-Patch: LVEF $\leq$ 0.35 and positive SAECG

ICD vs. Patches alone

ICD did not reduce mortality in pts having CABG

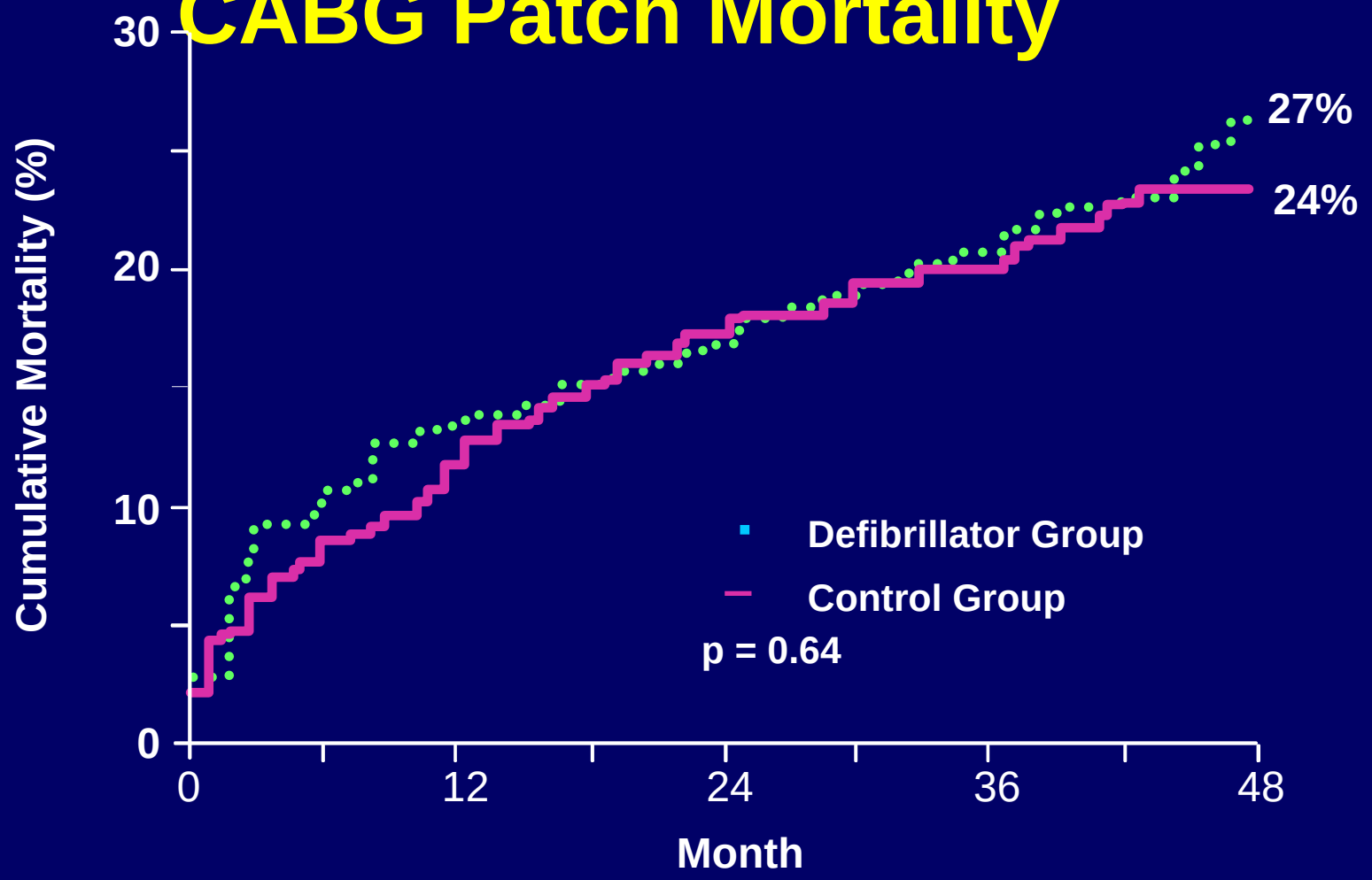
CABG changes the substrate and decreases risk

CABG Patch Enrollment Cascade



Bigger JT. N Engl J Med. 1997;337(22):1569-1575.

CABG Patch Mortality



Defibrillator Group	446	384	313	213	61
Control Group	454	399	308	199	57

Bigger JT. N Engl J Med. 1997;337(22):1569-1575.

Evidence-Based Medicine

AVID

CABG-Patch

MADIT

MUSTT

MADIT-II

DEFINITE

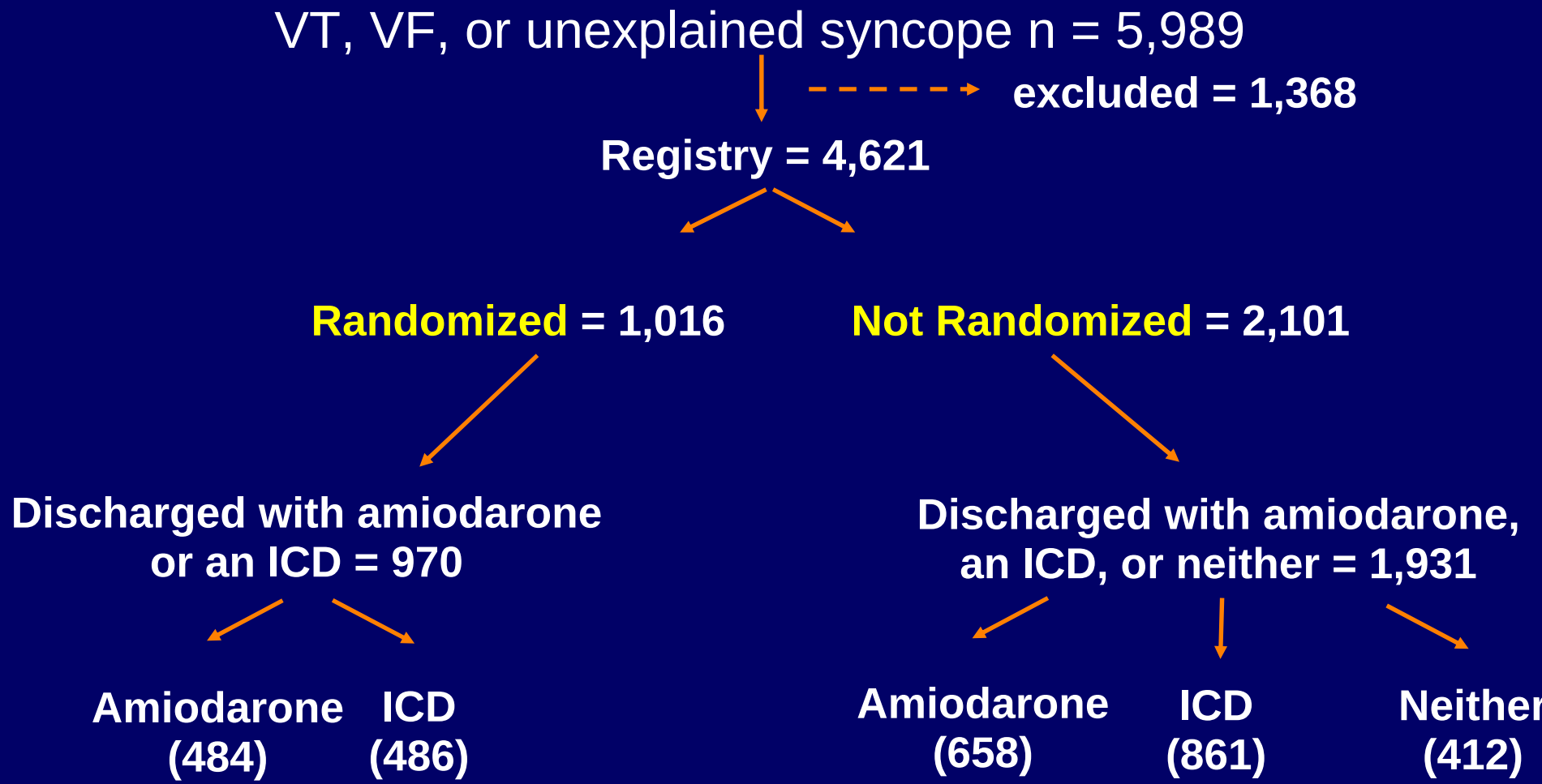
SCD-HeFT

Guided by clinical trials with all-cause death as the endpoint

Question 1: Secondary Prevention

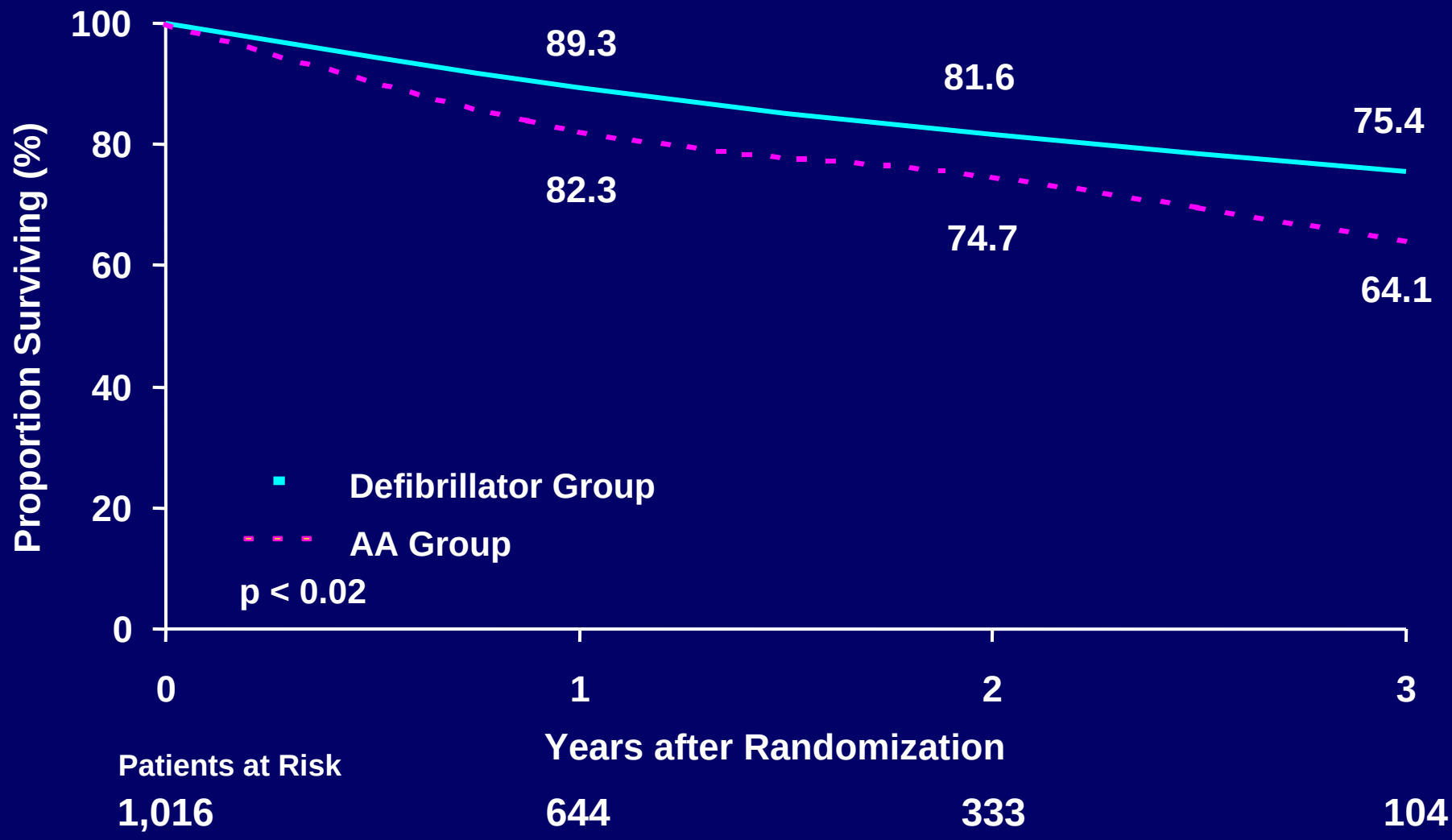
Does the ICD improve survival for patients with sustained Ventricular Arrhythmia?

Secondary Prevention: AVID



Adapted from: Exner DV, et al. J Am Coll Cardiol 1999; 34:325-333.

AVID Overall Survival

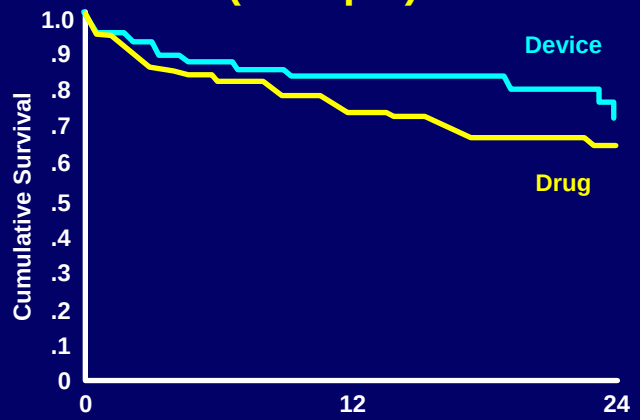


AVID Investigators. N Engl J Med. 1997;337(22):1576-1583.

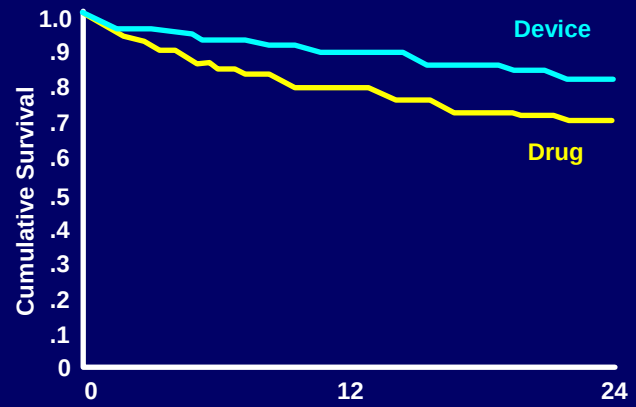
Survival in AVID Patients

Retrospective Stratification by EF

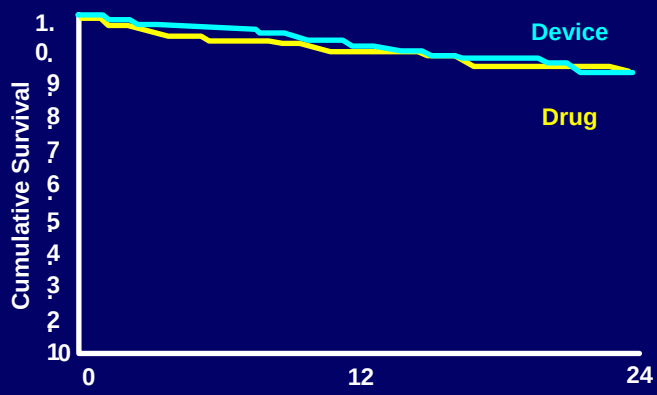
LVEF < 0.20
(Group 1)



LVEF 0.20 - 0.34
(Group 2)



LVEF > 0.34
(Group 3)



Patients with VF, symptomatic VT, asymptomatic VT, and syncope of unknown cause with significant heart disease and LV dysfunction

Domanski MJ, et al. J Am Coll Cardiol 1999; 34:1090-1095.

AVID Conclusions

The ICD improves survival in patients with LVEF < 0.35 and VT, VF, or VT-syncope.

ICD therapy did not improve survival in pts with moderate LV dysfunction (EF > 0.35).

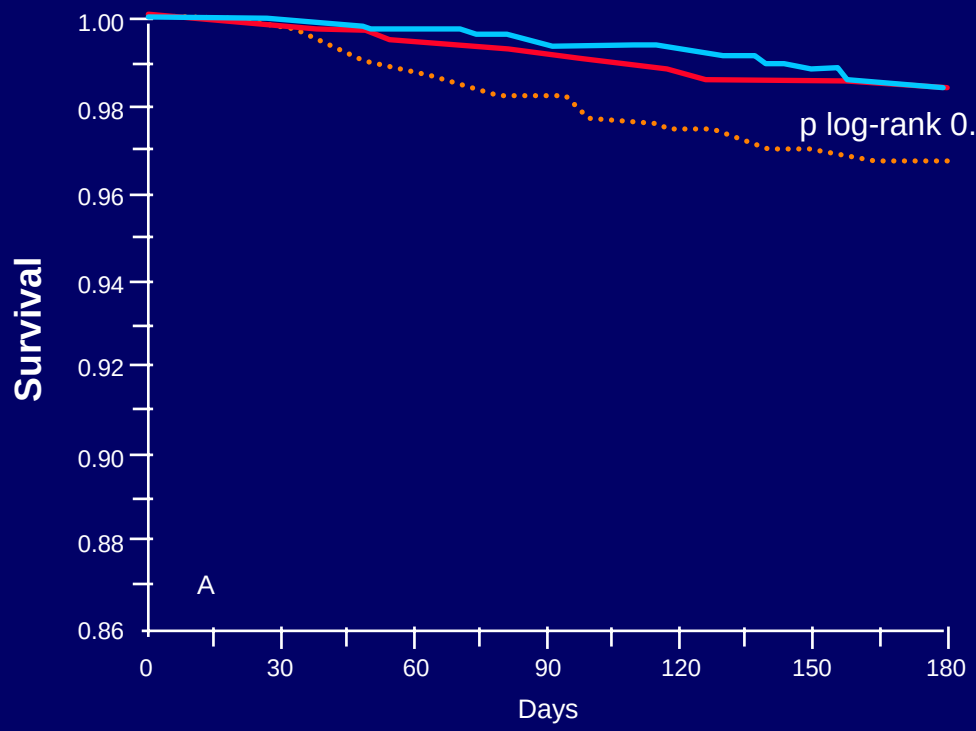
Domaski MJ, et al. J Am Coll Cardiol 1999; 34:1090-1095.

Primary Prevention of SCD

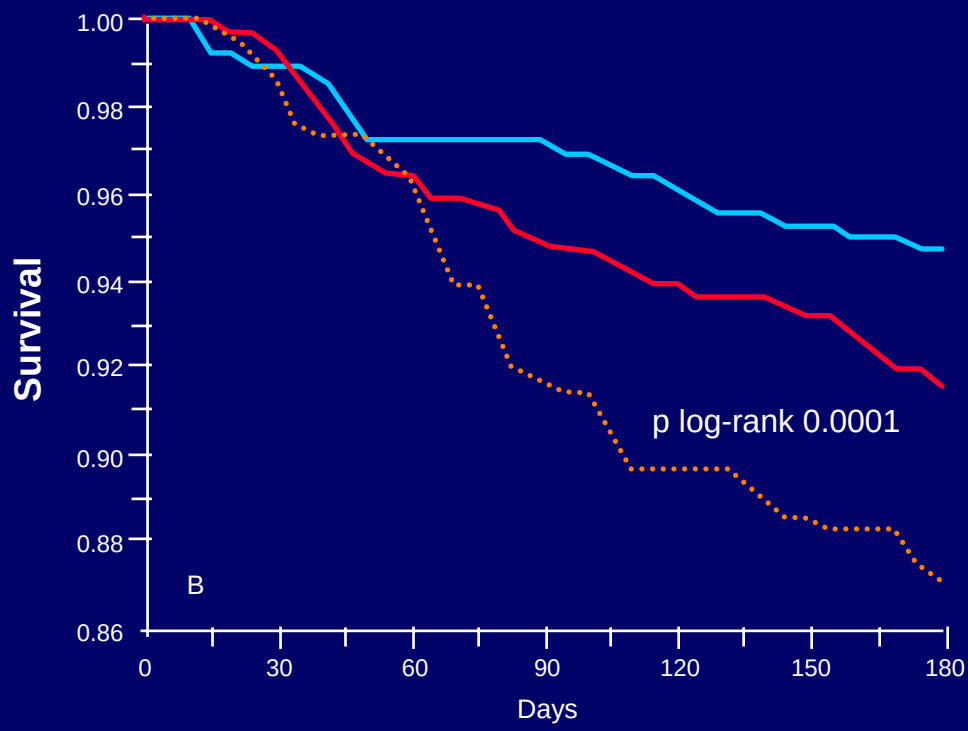
How to identify who is at greatest risk for SCD?

- **LV dysfunction, previous MI, and NSVT**
- **LV dysfunction, no history of MI, and NSVT**
- **LV dysfunction without arrhythmia or syncope**

GISSI-2: MI, PVCs, and SCD



Preserved EF



LV Dysfunction

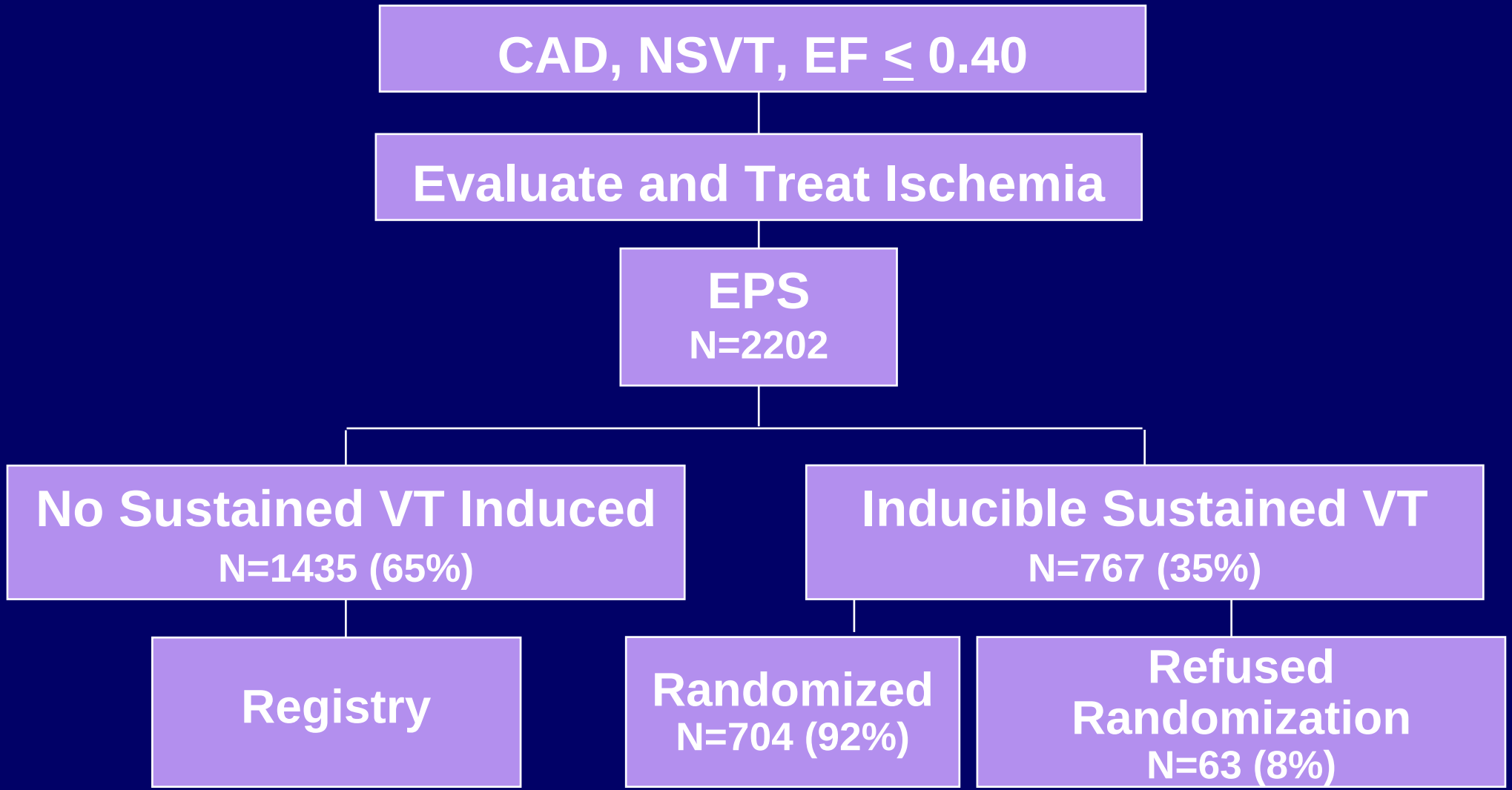
No PVCs
1-10 PVCs/h
> 10 PVCs/h

Maggioni AP. Circulation. 1993;87:312-322.

Question 2

Does the ICD improve outcomes in patients at NSVT and LV dysfunction due to MI who have not experienced sustained VT or VF?

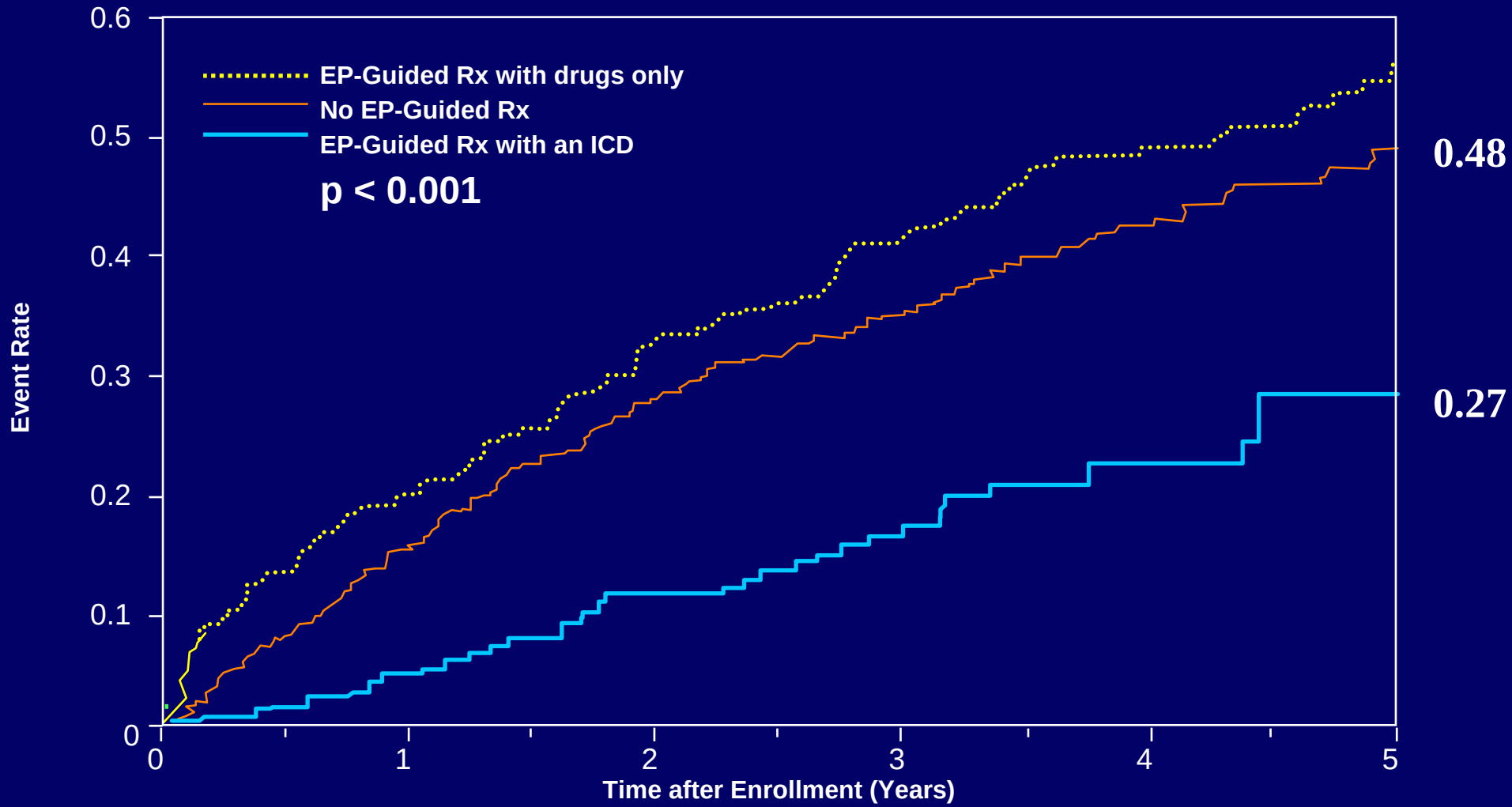
MUSTT: Initial Protocol



Buxton AE. *N Engl J Med*. 1999;341:1882-90.

MUSTT: Choice of Therapy for Induced VT

Absolute Mortality Difference 21%



Buxton AE. *N Engl J Med*. 1999;341:1882-90.

LV Dysfunction Not Due to MI

Patients with LV dysfunction without previous MI have an increased risk of SCD:

LVEF $\leq$ 0.35 and NSVT

Provocative testing has limited value in pts with non-ischemic LV dysfunction

DEFINITE: NSVT in Non-Ischemic CMP

ICD therapy vs. conventional medical therapy in patients with NSVT and LV dysfunction not due to CAD or previous MI

ICD reduced overall mortality: p=0.06

Kadish, NEJM 2004